

REMARKS

Claim Status

Claims 1, 2, 4, 11, 14, 25, and 26 are pending herein.

The Rejection Under 35 U.S.C. § 103(a)

Claims 1, 2, 4, 5, 11, 14, 15, 21, and 24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,994,329 (“Daifoitis”) in view of U.S. Patent No. 4,817,819 (“Kelly”) and separately in view of U.S. Patent 5,265,728 (“Allendorf”).

Daifoitis discloses bisphosphonate dosing according to a variety of dosing frequencies that are less frequent than daily dosing, for the purpose of minimization of gastrointestinal side effects. For example, Daifoitis discloses that its methods comprise a continuous dosing schedule selected from weekly dosing, twice-weekly dosing, biweekly dosing, and twice-monthly dosing (see Daifoitis at Column 4, lines 47 – 52). As such, other than disclosing dosing less frequent than daily dosing, there is little guidance or specificity regarding dosing frequency, and certainly no indication that any particular dosing regimen is critical or even important for the patient.

Even further, within the various disclosed continuous dosing schedules, it is clear that Daifoitis regards the days upon which dosing takes place, including intervals between bisphosphonate dosing, is also unimportant. To illustrate, Daifoitis discloses a dosing periodicity ranging from about once every 3 days to about once every 16 days (see Daifoitis Column 4, lines 53 – 56). Daifoitis then describes what is intended by once-weekly dosing, and states that the once-weekly dosing regimen can include a dosing regimen in which dosages of bisphosphonate are administered on two consecutive days falling within two different weekly periods. Daifoitis also describes twice-weekly dosing

of bisphosphonate in which each unit dosage of bisphosphonate is generally administered about every three to four days. The disclosure also states that the method can include administration on two consecutive days within a weekly period or different weekly periods. Daifoitis also discusses biweekly dosing, which is characterized as administration of bisphosphonate once during a two week period, which can be on non-consecutive days or consecutive days. Then Daifoitis further discloses twice-monthly dosing, by which is meant that a unit dosage of the bisphosphonate is administered twice during a monthly calendar period, on consecutive or non-consecutive days. This is distinguished from, and does not encompass, biweekly bisphosphonate administration because over a year period, about twenty-four dosages would be administered, whereas with a biweekly administration about twenty-six dosages would be administered. See Daifoitis, Columns 8 and 9.

Daifoitis also discloses a kit which “preferably includes a number of unit dosages”, without any specificity as to how many unit dosages of bisphosphonate or any recommendations or suggestions regarding structure of this kit, other than that it can include a card having the dosages in order of their intended use. Placebo dosages, or calcium or dietary supplements, can also be included. Importantly, there is no recognition or suggestion of whether the placebo or supplement should be administered concurrently with the bisphosphonate product, or at a different time or day. Rather, Daifoitis merely states the kit can include the vitamin or supplement with no further instruction or suggestion of its use. See Daifoitis, Column 13, lines 47 – 67.

Daifoitis is therefore clear that as long as the frequency of administration is less than daily dosing, there are no criticalities of frequency, nor are there criticalities regarding bisphosphonate intervals, which can be consecutive or non-consecutive. Furthermore, Daifoitis does not teach frequency of placebo or supplement administration, or when the placebo or supplement is administered relative to the bisphosphonate. As such, respectfully, it is inappropriate to conclude that there “are only a finite number of ways to arrange the pharmaceuticals and nutrients in the blister packs”; Daifoitis has so generally

disclosed so many frequencies, and so many intervals and orders of administration within those frequencies, as well as open-ended supplement administration, that little guidance is provided.

In contrast, instead of merely dosing less frequently on a relatively unspecified basis for the purpose of avoiding gastrointestinal effects, the present invention addresses a serious compliance issue which has been recognized as relevant to bisphosphonate dosing. For example, as stated in Applicants' specification, bisphosphonate products must be dosed at a different time or day relative to dosing of any other active products, such as nutrients; Applicants state that "the bisphosphonate and the calcium supplement should not be taken at the same time. Because bisphosphonates chelate calcium, taking a unit dose of a bisphosphonate at the same time as a calcium supplement interferes with the absorption of the bisphosphonate, thereby potentially decreasing the efficacy of the bisphosphonate." See Applicants' specification at page 2, line 28 through page 3, line 6. Moreover, because so many patients taking bisphosphonate products are also using calcium or other nutrients to supplement the bisphosphonate therapy, this is a widespread issue. As such, faced with requisite different dosing of a bisphosphonate *versus* a nutrient such as calcium, it is difficult for patients to develop, and practice, dosing regimens that result in efficacy for their osteoporosis therapy. The present invention as claimed addresses this issue through the development of a kit that specifically guides the patient through his or her therapy. Moreover, the kit is arranged such that the patient is guided to administer the nutrient subsequent to the active dose administration of the bisphosphonate. Again, because the nutrient must be dosed at a different time or even different day, this is critically important for compliance, and the specific arrangement of dosages as set forth in the present claims, addresses such compliance.

Each of Kelly and Allendorf fail to remedy the deficiencies of Dafoitis. Kelly and Allendorf are directed to blister packages for the continuous daily administration of birth control pills, the challenges of which bear no relation to the challenges of bisphosphonate dosing, particularly when such dosing is on a less than daily frequency with supplementation provided separate from such dosing. Applicants readily recognize these

deficiencies in its own specification; neither of these packages are “designed or intended to address the compliance issues associated with the continuous administration of a pharmaceutical active on a frequency other than daily together with taking a separate associated nutrient on the days in between the days the active ingredient is administered. The birth control pills are taken on a continuous basis on a 21-day or 28-day period instead of frequencies of less than daily. The challenges of bisphosphonate compliance on a less than daily basis are not remedied by packages which are designed to administer active drug every day for 21 or 28 days. Because Kelly and Allendorf do not address bisphosphonates administration, it is impossible to remedy the deficiencies of Daifoitis regarding specific frequency of bisphosphonate administration, interval between administration of each bisphosphonate dose, and supplement administration relative to bisphosphonate. It therefore follows that it would not have been obvious for one of ordinary skill to design the present kits based on the varied generalities of Daifoitis and teachings that are specific to continuous daily birth control administration as disclosed in Kelly and Allendorf.

In view of the foregoing, Applicants assert that the claims as amended herein would not have been obvious in view of Daifoitis and Kelly, or in view of Daifoitis and Allendorf, and the rejection should be withdrawn.

Conclusion

This response represents an earnest effort to place the present application in proper form and to distinguish the invention as claimed from the cited references. In view of the foregoing, reconsideration of this application and allowance of the pending claims are respectfully requested.

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Respectfully submitted,

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